ISSN: 2394-0026 (P)
ISSN: 2394-0034 (O)

Original Research Article

Bone marrow changes in elderly

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How to cite this article: M S Sulakshana, S M Ahmed, A R Raghupathi. Bone marrow changes in elderly. IAIM, 2015; 2(4): 27-33.

Available online at www.iaimjournal.com

Received on: 07-03-2015 **Accepted on:** 17-03-2015

Abstract

Aim: To study the bone marrow changes in elderly patients (above 60 years of age).

Material and methods: Bone marrow records from the pathology laboratory in the Department of Pathology, Bangalore Medical College, Bangalore, from March 2012 to June 2013, were searched, and cases from all patients at least 60 years old at the time of bone marrow study were retrospectively reviewed.

Results: During the 16 months period, 164 bone marrow examinations were performed, and out of these, 50 patients were at least 60 years old. The age range of the patients was 60 to 82 years, 27 were males and 23 were females. 47 cases (94%) yielded specific diagnosis. 27 cases (54%) had nutritional anemia, 6 cases (12%) were diagnosed as myeloma, 3 cases (6%) had aplastic anemia, 3 cases (6%) had chronic lymphocytic leukemia/ small lymphocytic leukemia infiltrating the bone marrow; 2 cases (4%) had acute myeloid leukemia, 2 cases (4%) had hypocellular marrow with myelofibrosis - grade 3, 2 cases were diagnosed to have monoclonal gammopathy of undetermined significance (4%), 1 case (2%) had metastatic deposits from prostatic carcinoma and 1 case (2%) had metastatic deposits from renal cell carcinoma - clear cell variant; 1 case (2%) of myelodysplastic syndrome - refractory cytopenia with multi lineage dysplasia and ringed sideroblasts was diagnosed.

Conclusions: In this study we found that after nutritional anemia, plasma cell dyscrasias were the most common findings in bone marrow studies in elderly patients. Diagnosis of plasma cell dyscrasias prompt for early institution of treatment resulting in reduced morbidity and mortality in such patients.

Key words

Elderly, Bone marrow, Cytopenia, Nutritional anemia, Plasma cell dyscrasias.

Introduction

Bone marrow examination is integral to the diagnosis of hematologic disorders and is also important to determine the stage and treatment of hematologic and other malignancies. The most common indications for bone marrow

ISSN: 2394-0026 (P)
ISSN: 2394-0034 (O)

examinations in general patient populations including children and adults are for the diagnosis and management of acute leukemia and staging for lymphoma [1, 2].

Little published literature is available regarding the indication and diagnostic usefulness of bone marrow biopsies specifically in the elderly population defined as patients 60 years or older. It seems likely that the indications and diagnoses made, as well as the impact of these diagnoses on therapy, would be different for this subpopulation. This information is of interest as the population India ages and the number of elderly patients undergoing bone marrow study may increase. It is of particular interest to our institution, a public tertiary care center in a state with one of the highest percentages of elderly people.

Increasing number of bone marrow aspirates and core biopsies are being done in elderly patients (above 60 years of age). Most of these patients present with anemia/ cytopenia. In elderly persons, the etiology of anemia differs sufficiently from the etiology in younger adults to warrant considering anemia in elderly persons as a distinct entity.

This study was done to determine the bone marrow changes in elderly patients (above 60 years of age) who presented with various signs/ symptoms, most commonly cytopenia.

Material and methods

Bone marrow records from the hematopathology laboratory in the Department of Pathology, Bangalore Medical College, Victoria Hospital, Bangalore, from March 2012 to June 2013, were searched, and cases from all patients at least 60 years old at the time of bone marrow study were retrospectively reviewed. Patient's age, sex, indication and clinical history provided by the patient's physician, and diagnosis were recorded for each of the cases.

The indications were classified into the following categories: cytopenias (1 or more); follow up of a previously diagnosed (before the age of 60 years) leukemia/ myeloma; suspicion of plasma cell myeloma; leukocytosis; follow-up or staging of a previously diagnosed lymphoma or chronic leukemia; or other, for indications that could not be placed in one of the previously named categories as per **Table - 1**.

Table - 1: Indications for bone marrow study in 50 cases.

Indications	**No. (%)**
Cytopenias	
• Bi/pancytopenia	27 (54)
• Anaemia **(Photo – 1A, 1B)**	23 (46)
• Thrombocytopenia	01 (2)
Suspicion of plasma cell myeloma	10 (20)
Suspicion of leukemia/ lymphoma	07 (14)
Follow up or staging of previously diagnosed case of leukemia/ lymphoma/ myeloma	03 (6)
Leukocytosis (Total count >1 lakh/ul)	02 (4)
Others	01 (2)

Results

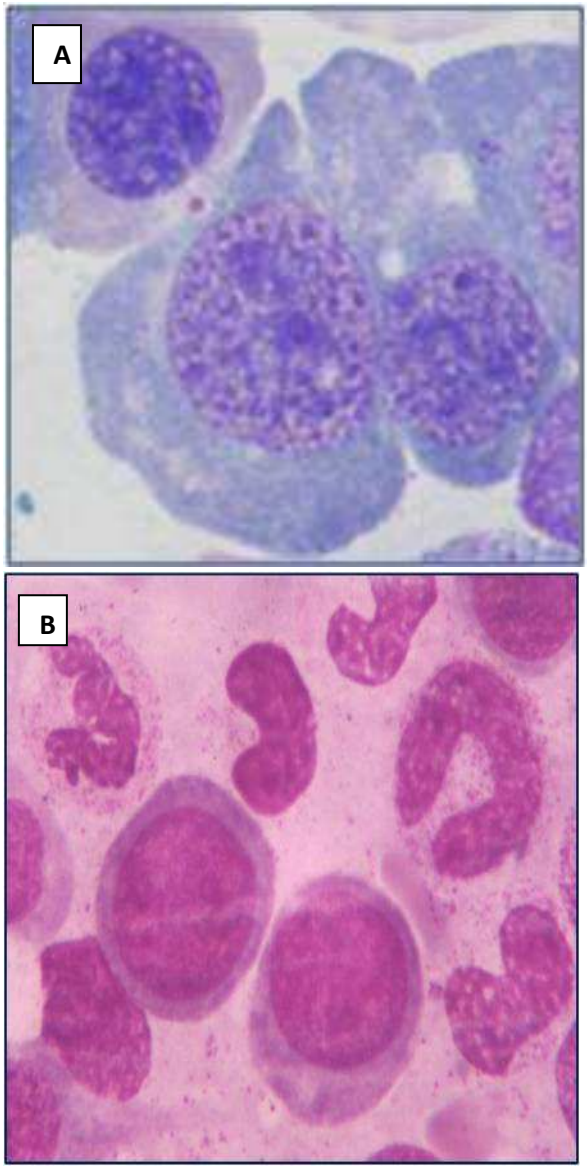
During the 16 months period, 164 bone marrow examinations were performed, and out of these, 50 patients were at least 60 years old. There were almost similar numbers of men (27) and women (23), and the age range of the patients was 60 to 82 years. In 30 patients, only bone marrow aspirations were done, and both aspiration and core biopsy was done in 20 patients.

In these patients, the hemoglobin levels ranged from 3.0 to 10.6 g/dL, platelet counts from 20,000 to 1.6 lac/µL, and white blood cell (WBC)

ISSN: 2394-0026 (P)
ISSN: 2394-0034 (O)

counts from 1,200 to 1.7 lacs/µl. Quantification of marrow iron stores was done by Perl's stain.

Photo – 1A, 1B: Bone marrow aspiration in Megaloblastic anemia showing megaloblasts and giant band form (Leishman's stain, 100X).



Excluding 3 bone marrow studies that were performed for follow-up or staging of previously known diseases, 47 cases (94%) yielded specific diagnosis. 27 cases (54%) had nutritional anemia (due to iron, Vitamin B12 and folic acid deficiency), 6 cases (12%) were diagnosed to have myeloma, 3 cases (6%) had aplastic anemia, 3 cases (6%) were diagnosed to have chronic lymphocytic leukemia/ small lymphocytic leukemia infiltrating the bone marrow; 2 cases (4%) had acute myeloid leukemia, 2 cases (4%) of hypo cellular marrow with myelofibrosis - grade 3 were reported, 2 cases were diagnosed to have monoclonal gammopathy of undetermined significance (MGUS) (4%), 1 case (2%) had metastatic deposits from prostatic carcinoma and 1 case (2%) had metastatic deposits from renal cell carcinoma - clear cell variant; 1 case (2%) of myelodysplastic syndrome - refractory cytopenia with multi lineage dysplasia and ringed sideroblasts was diagnosed as per **Table - 2**.

Discussion

It seems that the indications and diagnostic usefulness of bone marrow studies in elderly patients differ from those of bone marrow studies in patient populations composed of children or young to middle-aged adults. Studies of general patient populations have shown that the most common indications for bone marrow study include diagnosis and management of acute leukemia and staging for lymphoma.

In this study, cytopenias were the most common indication, accounting for 54% of the cases. Other common indications in this study, including suspicion of plasma cell myeloma, leukocytosis, and follow-up of a known plasma cell myeloma, were rarer indications in general patient populations. Few marrow studies were performed for suspicion of acute leukemia and metastasis.

Excluding the biopsies for follow-up or staging of previously known diseases, plasma cell dyscrasias (myeloma and MGUS) were the most common new diagnoses in patients at least 60 years old, accounting for almost 16% of all new diagnoses. This finding differs significantly from

ISSN: 2394-0026 (P)
ISSN: 2394-0034 (O)

the previously referenced studies of biopsies in general hospital populations, in which the most common diagnoses were acute leukemias and lymphomas, although it is unclear if these studies included repeated biopsies during therapy and staging of leukemia and lymphoma in their numbers [3].

Table - 2: Specific diagnoses made on bone marrow aspirations/ biopsy.

Diagnosis	No
Multiple myeloma **(Photo – 2)**	06
Monoclonal gammopathy of undetermined significance **(Photo – 3)**	02
Chronic lymphoid leukemia/ Small lymphocytic leukemia	03
Acute myeloid leukemia	02
Aplastic anaemia **(Photo – 4A, 4B)**	03
Myelofibrosis	02
Metastatic deposits - Prostatic carcinoma **(Photo – 5)**	01
Metastatic deposits - Renal cell carcinoma	01
Myelodysplastic syndrome (MDS) - Refractory cytopenia with multi lineage dysplasia and ringed sideroblasts **(Photo – 6, Photo - 7)**	01

Photo - 2: Multiple myeloma - Bone marrow biopsy showing increased number of plasma cells (H&E stain, 40X).

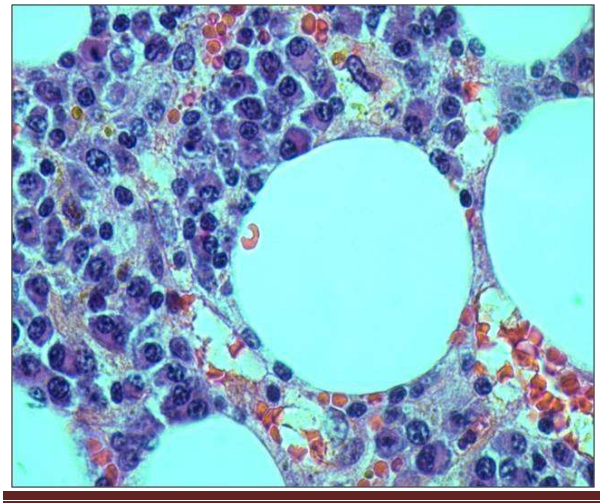


Photo – 3: Bone marrow aspiration showing increased number of plasma cells in MGUS (Leishman's stain, 40X).

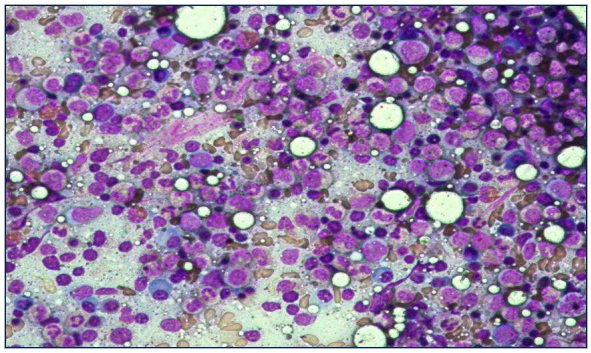
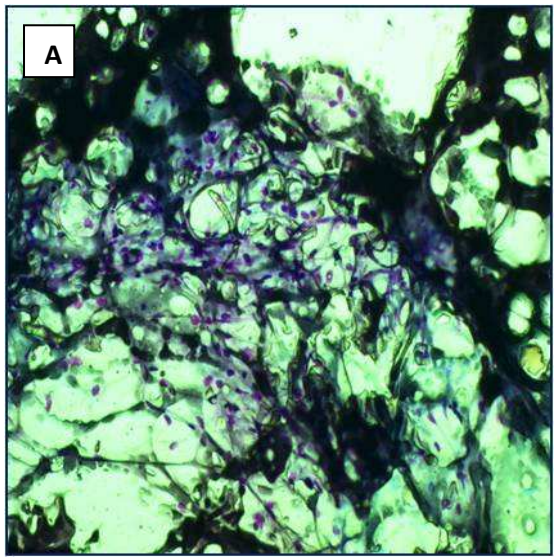


Photo – 4A, 4B: Bone marrow aspiration in Aplastic anemia - increased fat spaces, lymphocytes and mast cells (Leishman's stain, 10X and 40X)



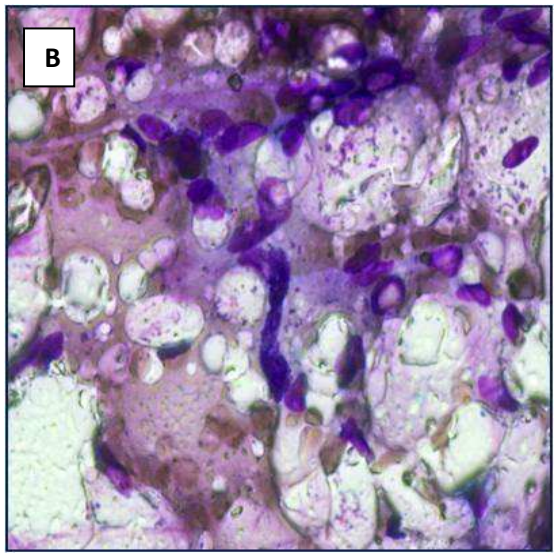


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Photo – 5: Prostatic carcinoma metastatic deposits in bone marrow biopsy (H&E stain, 40X).

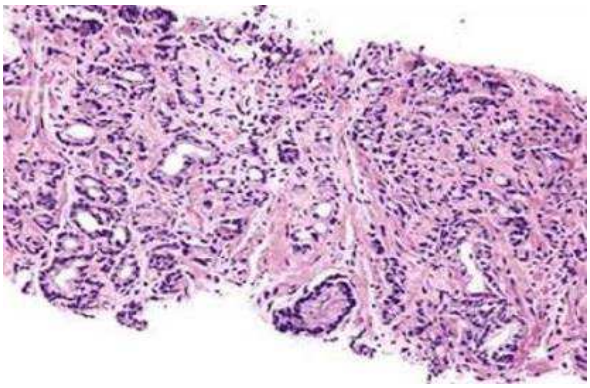


Photo – 6: Bone marrow aspiration in MDS showing megaloblasts, dyserythropoiesis and Pawn ball megakaryocyte (Leishman's stain, 40X).

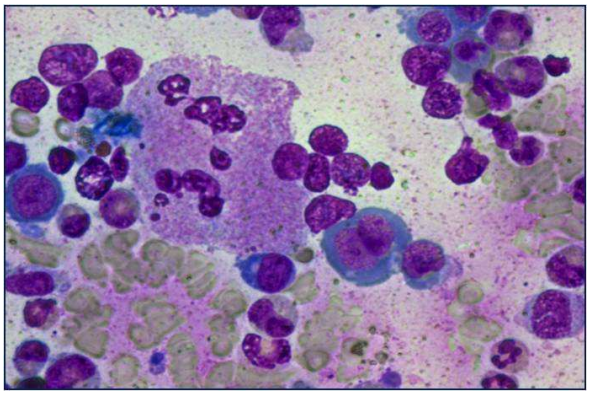
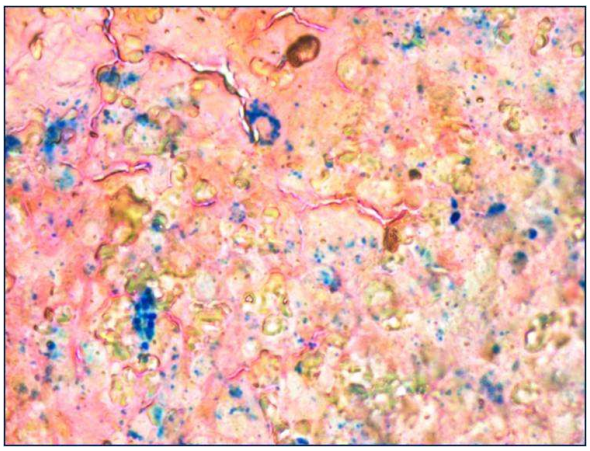


Photo – 7: Bone marrow aspiration in MDS showing increased iron stores and a ringed sideroblast (Perl's stain, 40X).



Multiple myeloma is a disseminated malignancy of monoclonal plasma cells that accounts for 1.3% of all malignancies and 15% of hematologic cancers. The incidence has been increasing by 0.7% each year for the last 10 years while mortality has come down by 1.7% each year over the same period. The incidence rate was 5.9 (7.4 in men and 4.7 in women) and the number of deaths was 3.4 per 100,000 persons per year (4.4 in men and 2.7 in women). Widespread use of the immunomodulatory drugs and proteasome inhibitors over the past decade has resulted in improved life expectancy, with a median survival beyond 5 years. The prevalence of multiple myeloma has increased, and currently an estimated 77,600 people in the United States live with myeloma [4].

In this study, the indications that resulted in the highest yield of specific diagnoses in bone marrow studies were M spike in serum protein electrophoresis and leukocytosis. Cytopenias, while the most common indication, resulted in the lowest diagnostic yield.

The marrow is approximately 100% cellular during the first three months of life, 80% cellular in children through age 10 years; it then slowly declines in cellularity until age 30 years, when it remains about 50% cellular. The usually accepted range of cellularity in normal adults is 40–70%. The marrow cellularity declines again in elderly patients to about 30% at 70 years. Although it is known that the hematopoietic system is modestly affected by age as indicated by the continuous decrease in bone marrow hematopoietic elements, normal aging does not cause significant decreases in blood cell count parameters [5, 6, 7, 8, 9, 10]. However, anemia is very common in elderly patients and is considered an important cause of morbidity. Even mild anemia has been shown to have a significant impact on the quality of life in elderly patients.

ISSN: 2394-0026 (P)
ISSN: 2394-0034 (O)

In an elderly patient with anemia, bone marrow examination would ideally be used to exclude or confirm the diagnosis of myelodysplasia or other serious hematolymphoid disease and to help guide therapy.

Causes of anemia in the population over age 65 years are relatively few. According to an analysis of the Third National Health and Nutrition Examination Survey (NHANES III), 34% of anemia in older adults was due to folate, B12, or iron deficiency alone or in combination. Iron deficiency is frequently seen in the elderly and usually is a result of acute or chronic blood loss through the gastrointestinal tract. Anemia of chronic disease is associated with several conditions more common in older persons: inflammatory conditions, malignancy, diabetes, heart failure, stroke, liver and renal diseases. Autoimmune destruction of IF-secreting parietal cells, or pernicious anemia, accounts for approximately 2% of the population over age 60 years. Atrophic gastritis and hypo chlorhydria may progress with advancing age and may be partly responsible for the 12% of patients over age 75 years who will have a low B12. The majority of older patients with vitamin B12 deficiency are found to malabsorb dietary protein-bound vitamin B12. Post-gastrectomy states, pancreatic insufficiency, and disease or resection of the terminal ileum also impair absorption of B12. In most studies, 15-30% of patients studied will not have an explanation for their anemia [11, 12].

A well-known etiology of anemia that increases with age is myelodysplasia (MDS). Occult MDS may be an important cause of “unexplained” anemias in the elderly. At this point in time, MDS requires bone marrow aspiration and biopsy for clinical confirmation. This goal can be a complicated task because at least one study has shown that dysplastic changes are observed more frequently in bone marrow biopsy specimens of patients 60 years or older [13, 14]. In our study, we found a case of Myelodysplastic syndrome - Refractory anemia with multi lineage dysplasia and ringed sideroblasts in an elderly male presenting with pancytopenia.

Primary myelofibrosis usually presents in individuals above 60 years of age and 33% of these are asymptomatic. In our study, two patients were diagnosed to have myelofibrosis and both presented with only anemia.

In this study we found that after nutritional anemia, plasma cell dyscrasias were the most common findings in bone marrow studies in elderly patients. Out of 6 patients who were diagnosed to have Plasma cell myeloma, 3 were male and 3 were female. All six cases presented with M spike in serum protein electrophoresis, had lytic bone lesions and renal involvement. Hence, early diagnosis and treatment in these cases can significantly decrease the morbidity and mortality in these patients.

In adults, the tumors most often seen metastasizing to bone marrow are carcinomas of the prostate gland, breast, lung, thyroid and kidney. In our study, we found a case each of prostate carcinoma and renal cell carcinoma-clear cell variant metastasizing to bone marrow.

Although bone marrow biopsies are safe, with reported complication rates of 0.05%, it might be suggested that age-related frailty may result in increased morbidity from bone marrow biopsies, although data on age-related incidence of bone marrow complications are sparse [3, 6, 15]. A large study in 2003 that looked at bone marrow biopsy morbidity and mortality did not report the age of patients who experienced complications but concluded that MPNs, diseases increasingly common in elderly patients, were one of the most common potential risk factors [15].

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Conclusion

Changes due to nutritional anemias and plasma cell dyscrasias have been found to be the most common pathologies in the bone marrows of elderly patients. Patients with poor performance status or mild decreases in CBC count parameters or in whom there is a low suspicion for high-grade clonal neoplasms may benefit from simple supportive therapy and follow-up to avoid the cost and potential morbidity from bone marrow aspiration/ biopsy. However, diagnosis of plasma cell dyscrasias on bone marrow aspirations/ biopsies prompt for early institution of treatment resulting in reduced morbidity and mortality in such patients.

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Source of support: Nil **Conflict of interest:** None declared.